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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/620,852	07/15/2003	Mark Chee	67234-015	2545

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MCDERMOTT, WILL & EMERY
4370 LA JOLLA VILLAGE DRIVE, SUITE 700
SAN DIEGO, CA 92122

EXAMINER	
TUNG, JOYCE	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/620,852	CHEE ET AL.	
	Examiner	Art Unit	
	Joyce Tung	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-103* is/are pending in the application.

4a) Of the above claim(s) *33-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The applicant's response filed 1/12/07 has been entered, Claims 1-103 are pending. Claims 33-52 are examined.

1. The rejection of claims 35-52 under 35 U.S.C. 112, second paragraph, is withdrawn because of the amendment.

2. Claims 35-52 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5, 6, 11, and 13-30 of copending Application No. 10194958 because the terminal disclaimer was not filed.

3. Claims 35, 39, 41, 42, 43, 44, 47, and 49 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 10, 18, 20-22, 23-24, 32, 39-40, 42-46, 54, and 64-66 of copending Application No. 10864935 because the terminal disclaimer was not filed.

4. Applicant's arguments with respect to claims 33-52 under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) respectively in view of Phillip Morris et al. (6,017,738, issued January 25, 2000), Barany et al. (6,027,889, issued February 2000), and Akhavan-Tafti (5,998,175, issued December 7, 1999) have been considered but are moot in view of the new ground(s) of rejection.

NEW GROUNDS OF REJECTION NECESSITATED BY THE AMENDMENT

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 35-46 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) in view of Phillip Morriss et al. (6,017,738, issued January 25, 2000) and Barany et al. (2002/0150921, issued Oct. 17, 2002).

Bhatnagar et al. disclose a process for amplifying nucleic acid sequence from a DNA or RNA template. The process allows to efficiently detect a particular point mutation (See the abstract). The process provides primers comprising a first primer which is substantially complementary to first segment at a first end of the target nucleic acid sequence and a second primer, which is substantially complementary to a second segment at a second end of the target nucleic acid sequence. The first and second primers are hybridized to the target nucleic acid sequence (See column 3, lines 11-30). The second primer (oligo 2) is extended and then ligated to the first primer (See fig. 3) to produce fused amplification products (See column 3, lines 31-34). The fused amplification products are amplified (See column 3, lines 35-44). The process also provides four different nucleotide bases (See column 3, lines 27). The amplified fused amplification products are detected by detectable signal (See column7, lines 8-22). The primers

may be labeled using a marker (See column 9, lines 17-23, column 15, lines 17-54). The amplified stands may be labeled with different markers (See column 9, lines 24-29). The extension of a primer by polymerase can be blocked (See column 7, lines 32-39).

Bhatnagar et al. do not explicitly disclose linear amplification of the first and second ligated probe to produce first and second amplicons. However, in the disclosure of Bhatanagar et al. the fused amplification product is dissociated from the target nucleic acid sequence and then the fused amplification product is extended by a third primer (See column 3, lines 36-44). It is inherent in the teaching that this step is single primer amplification, which is linear amplification.

Bhatnagar et al. also do not explicitly disclose a universal priming site in a probe. Based on the definition in the specification, the universal priming site means a sequence of the probe, which will bind to a primer for amplification (See 20040121364, [0084]). Thus the features of the primers of Bhatanagar et al. satisfy the limitations of the probe of the instant invention.

Bhatnagar et al. also do not explicitly disclose a second universal priming site in the first probe or second probe. Based upon the discussion above and no physical requirements for the second universal priming site, the first and the second probe are interpreted that the first or second probe has a second universal priming site.

Bhatnagar et al. do not disclose determining a relative amount of the first and second amplicons and the universal priming site comprising a RNA polymerase priming site corresponding to T7, T4 T3, and SP6 RNA polymerase.

Phillip Morriss et al. disclose a method for detecting a target nucleic acid sequence in which a first primer hybridizing to the target nucleic acid sequence is immobilized and a second primer is provided to hybridize the target nucleic acid sequence in the opposite direction and the

second primer is labeled (See the Abstract). The incorporated label in the amplified nucleic acid sequence allows detection and quantification of the amplified nucleic acid (See column 2, lines 1-15). The nucleic acid amplification methods applied to the solid phase amplification process (See column 6, lines 41-58) include NASBA. NASBA amplification method has a transcription step in vitro (See fig. 3). The primer used in NASBA has a RNA promoter sequence corresponding to T7 RNA polymerase (See column 7, lines 12-18). This teaching reads on the limitation recited in claims 36 and 37 in which universal priming site comprises a RNA polymerase priming site corresponding to T7, T4, T3, SP6 RNA polymerase.

One of ordinary skill in the art at the time of the instant invention would have been motivated to apply the method of Bhatnagar et al. to determine the amount of the first amplicon and the second amplicon because as disclosed by the teachings of Philip Morriss et al. the incorporated label in the amplified nucleic acid sequence allows detection and quantification of the amplified nucleic acid (See column 2, lines 1-15). It would have been prima facie obvious to determine the relative amount of the first and the second amplicons for detecting the relative amount of two or more target sequences.

None of the references above discloses the target nucleic acid sequences comprise a solid support, immobilizing the amplification templates or amplicons to a solid support with a capture probe, and that the ligation probes comprise an adapter sequence that differs from the first and second target sequences.

Barany et al. disclose a method for identifying one or more of a plurality of sequence differing by one or more single base changes (See pg. 3, [0027]]. The method also provides quantitave detection of mutations in a high background of normal sequence (pg. 4, {0035]). The

method applies a first oligonucleotide probe having a target specific portion and an addressable array-specific portion and second oligonucleotide probe having a target-specific portion and a detectable reporter label. When hybridized adjacent to one anther on a corresponding target nucleotide sequence the first and the second oligonucleotide probe are suitable for ligation together. The ligated products contain the addressable array-specific portion. If there are one or more mismatches, the oligonucleotide probes may hybridize to nucleotide sequence in the sample other than their respective target sequences (See pg. 3, [0028]). After ligation phase, the ligated products are captured on an addressable array in which a capture probe is immobilized at particular sites and the addressable array-specific portion is complementary to the capture probe (See pg. 3, [0029]). It is inherent in the teaching that the probe has a different sequence, which differs from a target (See the Abstract).

One of ordinary skill in the art would have been motivated to apply the addressable array-specific portion to the probe of Bhatnagar et al. used as an adapter sequence because by doing so, the method provides quantitative detection of mutations in a high background of normal sequence (See pg. 4, [0035]). It would have been prima facie obvious to apply the first probe or the second probe with the adapter sequence that comprises different sequences from the target sequences to make the instant invention.

One of ordinary skill in the art would have been motivated to apply the addressable array-specific portion as taught by Barany et al. to the probe of Bhatnagar et al. used as an adapter sequence because by doing so, the method provides quantitative detection of mutations in a high background of normal sequence (See pg. 4, [0034]). It would have been prima facie obvious to apply the first probe or the second probe with the adapter to make the instant invention.

7. Claims 47-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bhatnagar et al. (5,593,840, issued January 14, 1997) in view of Phillip Morriss et al. (6,017,738, issued January 25, 2000) and Barany et al. (2002/0150921, issued Oct. 17, 2002) as applied to claims 35-46 and 49-52 above, and further in view of Akhavan-Tafti (5,998,175, issued December 7, 1999).

The teachings of Bhatnagar et al. Philip Morriss et al. and Barany et al. are set forth in section 6 above. Bhatnagar et al., Philip Morriss et al. and Barany et al. do not disclose a plurality of pairs of ligation probes with a plurality of target sequences to form a plurality of ligation complexes, each of the plurality comprises more than two and the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536.

Akhavan-Taffti discloses a method of synthesizing polynucleotides involving the simultaneous ligation of a set of oligomer 5'-phosphates onto a template-bound primer. The ligation is performed with a ligase enzyme (See the abstract). It is inherent in this teaching that a plurality of pairs of ligation probes with a plurality of target sequences is to form a plurality of ligation complexes and each of the plurality comprises more than two (See fig. 2). The disclosure of Akhavan-Taffti also discussed the library can contain all 4^n possible oligomers (See column 5, lines 55-59 and column 6, lines 22-43).

One of ordinary skill in the art would have been motivated to apply a plurality of pairs of ligation probes with a plurality of target sequences to form a plurality of ligation complexes in which the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536 as taught by Akhavan-Taffti because the amplification method of Akhavan-Taffti can be use to copy DNA or RNA linearly or exponentially (See column 1, lines 15-17). It would have been prima facie

obvious to apply a plurality of pairs of ligation probes with a plurality of target sequences to form a plurality of ligation complexes in which the plurality of probes comprises at least 8, 96, 192, 384, 1152 or 1536.

Summary

8. No claims are allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
March 26, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

3/29/07